REMARKS

Please reconsider this application in view of the above amendments and the following remarks. Applicant thanks the Examiner for carefully considering this application.

Disposition of the Claims

Claims 1-3 and 5-71 are pending. Claims 26-52 have been withdrawn. Therefore, claims 1-3, 5-25, and 53-71 are under consideration. Claims 1, 2, 10, 14, 53, and 57 are independent. The remaining claims depend, directly or indirectly, from these independent claims.

Claim Amendments

Claims 2, 12, 24, 55, and 70 have been amended to delete "metabolic syndrome." Claim 7 is amended to recite "insulin resistance" instead of "metabolic syndrome." Claims 5-9 have been amended to correct dependency. Claims 10, 14, and 15 have been amended to correct typographic errors. No new matter is introduced by these amendments.

Claim Rejections under 35 U.S.C. § 112

Claims 1-3, 5-9, 12, 24, 55, and 70

Claims 1-3, 5-9, 12, 24, 55, and 70 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for simultaneous treatment and prevention of the remaining disorders of these claims. This rejection is respectfully traversed.

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). A patent need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986); *see also*, MPEP § 2182.

The following are Applicant's comments with respect to the Wands factors:

(1) the nature of the invention and (2) the breadth of the claims:

The claims are drawn to compounds of formula (I) and methods for treating a disease mediated by SCD. Applicant respectfully notes that the claims do not require "simultaneous treatment and prevention" of a disease mediated by SCD. (see below).

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The Examiner cites Dobrzyn et al. as teaching future research is needed. While that general statement may be true (because scientific pursuit is often not finished), that is not what Dobrzyn et al. actually teaches. In fact, Dobrzyn et al. teaches that "Stearoyl-CoA desaturase (SCD), the rate-limiting enzyme in monounsaturated fatty acid synthesis, has recently been shown to be the critical control point regulating hepatic lipogenesis and lipid oxidation. As several manifestations of the metabolic syndrome and type 2 diabetes mellitus are associated

with alterations in intracellular lipid partitioning, we propose that SCD1 may be a potential therapeutic target in the treatment of obesity and the metabolic syndrome. In support of this notion, we have shown that SCD1-deficient mice have increased energy expenditure, reduced body adiposity, increased insulin sensitivity and are resistant to diet-induced obesity and liver steatosis." (Abstract). (emphasis added). Thus, Dobrzyn et al. showed that inhibition or reduction of SCD activity can be used to treat various SCD-mediated metabolic disorders.

Furthermore, other prior art references, listed in the Applicant's Response to Office Action dated June 24, 2009 (pages 31-33), also teach that reduction or elimination of SCD-1 can help relieve the disease or condition. For example, Park, E.I. *et al.*, *J. Nutr.* (1997), Vol. 127, pp. 566-573, shows that mice provided with a diet that lowered the expression of SCD-1 had lower body weight and lower serum concentrations of total cholesterol, triglycerides, and HDL cholesterol. Miyazaki, M. *et al.*, *Journal of Lipid Research* (2001), Vol. 42, pp. 1018-1024, shows that triglyceride synthesis was dramatically reduced in the liver of SCD-deficient mice fed a lipogenic diet compared to normal mice. (*See* also Miyazaki, M. *et al.*, *J. Biol. Chem.* (2000), Vol. 275, No. 39, pp. 30132-30138.) Zheng *et al.*, *Nat. Genet.* (1999) 23:268-270, showed that rodents lacking a functional SCD1 gene had changes to the condition of their eyes, skin and coat thereby reducing the excessive sebum production that typically results in the formation of acne. Therefore, the prior art is replete with evidence that inhibition or reduction of SCD activity can be used to treat SCD-mediated disorders.

The examiner asserts that Ntambi teaches that future research is required for viable target of SCD inhibition. However, Ntambi does not study the link between inhibition of SCD activity and treatment of SCD-mediated diseases. Instead, Ntami shows that both polyunsaturated fatty acids (PUFAs) and cholesterol can control the synthesis of monounsaturated fatty acids in liver by regulating the expression of the SCD genes. Even though Ntambi states that further elucidation of the mechanisms by which PUFA and cholesterol alter cellular monounsaturated fatty acids is needed to understand the impact of SCD gene regulation in various human disease states, this does not contradict with the effectiveness of SCD inhibition in the treatment of SCD-mediated diseases.

The Examiner also asserts that "[t]he simultaneous treatment and prevention of a disease is not possible. If a person already has a disease, only alleviation is possible. If a subject does not have a disorder, only prevention is possible." (Final Office Action, page 4).

The claims do not recite "simultaneous treatment and prevention," as asserted by the Examiner. Instead, the claims recite methods of treating a disease or condition mediated by SCD. The specification defines "treating" or "treatment" as follows:

"Treating" or "treatment" as used herein covers the treatment of the disease or condition of interest in a mammal, preferably a human, having the disease or disorder of interest, and includes:

(i) preventing the disease or condition from occurring in a mammal, in particular, when such mammal is predisposed to the condition but has not yet been diagnosed as having it;

(ii) inhibiting the disease or condition, *i.e.*, arresting its development; **or**

(iii) relieving the disease or condition, *i.e.*, causing regression of the disease or condition.

(Specification, page 27, lines 3-11) (emphasis added).

(5) The relative skill of those in the art:

Applicant agrees with the examiner that one skilled in the art is MD's, PhD's, or those with advanced degrees and the requisite experience in the treatment of a disorder medicated by SCD. With such high levels of training and experience, one skilled in the art can easily practice the invention as described without undue experimentation.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The examiner admits that the specification has provided guidance for in vitro inhibition of SCD with the compounds of the invention. As noted above and in our previous responses, the prior art is replete with evidence of the effectiveness of SCD inhibition in the treatment of SCD-mediated diseases. Therefore, the present description, in combination with the prior art, enables one skilled in the art to use compounds of the invention to treat an SCD-mediated disease or disorder without undue experimentation.

(8) The quantity of experimentation necessary:

As noted above, the prior art is replete with evidence supporting the effectiveness of SCD inhibition in the treatment of SCD-mediated diseases; the field is relatively mature and

predictable. In light of this and the guidance provided in the specification, one skilled in the art can make and use the invention without undue experimentation.

In sum, a skilled artisan familiar with the prior art would reasonably expect that compounds of the invention can be used to "treat" (i.e., "prevent" **or** "relieve") a disease or condition mediated by SCD-1 without undue experimentation. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 2, 3, 7, 12, 24, 55, and 70

Claims 2, 3, 7, 12, 24, 55, and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner asks what metabolic syndrome is being treated. This rejection is respectfully traversed.

"Metabolic syndrome" is also referred to as "insulin resistance syndrome," which is a group of conditions that cause a person to be at risk for heart disease and diabetes. These conditions include high blood pressure, high blood sugar levels, and high levels of triglycerides. (*See* http:/www.nlm.nih.gov/medlineplus/metabolicsyndrome.html). Therefore, one skilled in the art would not consider "metabolic syndrome" indefinite.

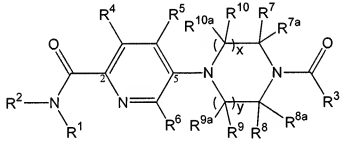
However, in the interest of expediting the prosecution of this application, the claims have been amended to delete "metabolic syndrome." Accordingly, withdrawal of this rejection is respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 57, 58, 61, and 71

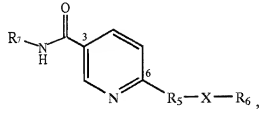
Claims 57, 58, 61, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (U.S. Patent No. 6677452) (hereinafter "Chen"). This rejection is respectfully traversed.

Claim 57 is directed to compounds of the following structure (formula VIb):



(VIb)

Chen discloses nicotinamde compounds. The compounds (Example I, Col. 31-32) cited by the examiner have the following general structure:

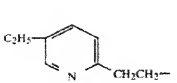


wherein R_5 is piperazine, X-R_6 is benzoyl, and R_7 includes various groups. Notably, these compounds have the carboxamide attached to the C-3 position of the pyridine ring and the piperazine attached to the C-6 position of the pyridine ring. In contrast, compounds of formula (VIb) in the present claims have the carboxamide attached to the C-2 position of the

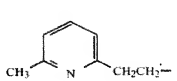
pyridine ring and the piperazine attached to the C-5 position of the pyridine ring. These are non-trivial variations. In addition, Chen teaches these compounds for different uses (treatment of pain or infection, acaricide, and antimicrobial, as noted by the examiner).

In a post *KSR* decision, the Federal Circuit held: "[a] known compound may suggest its homolog, analog, or isomer because such compounds 'often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.' We clarified, however, that in order to find a *prima facie* case of unpatentability in such instances, a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention' was also required. *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.* (Fed. Cir. 2006-1329; June 28, 2007). (citations omitted)." (Emphasis added).

In the *Takeda* case, the obviousness is a much closer issue than the present case, and yet the Federal Circuit found that Takeda's compound (structure shown below; left), which has an ethyl group attached to the 5-position of the pyridine ring, is not rendered obvious by a prior art compound having a methyl attached to the 6-position of the pyridine ring (shown below; right) because the prior art does not suggest the particular modification necessary to achieve the claimed compound.



Takeda's compound



Prior art

In a more recent case, the Federal Circuit reiterated this standard: under KSR, "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *The Procter & Gamble Company v. Teva Pharmacruticals USA, Inc.*, 2009 WL 1313321 (Fed. Cir. 2009) (citing *Takeda*).

The structural difference between the compounds of the present invention and the compounds in Chen is more pronounced than that in the *Takeda* case. Chen also does not teach or suggest the particular modification necessary to achieve the compounds of the present invention. Therefore, Chen cannot render compounds of the present invention obvious.

Furthermore, Chen discloses these compounds for different uses. Chen does not teach or suggest any of these compounds can be used to inhibit SCD. The Examiner asserts that the compounds of Chen, although used for a materially different purpose than the instant application, would be obvious to try as inhibitors of SCD. (Final Office Action, page 7).

However, 'obvious to try' rationale may support a conclusion that a claim would have been obvious where one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success." *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727; 82 USPQ2d 1385, 1397 (2007)." (Emphasis added).

Applicant does not understand why it would be "obvious to try" the compounds of Chen as inhibitors of SCD with a reasonable expectation of success, when there are many

hundreds or thousands of different enzymes (not a finite number of identified, predictable solutions) in a biological system and there is no guidance provided by Chen. If the examiner bases this assertion on personal knowledge, Applicant respectfully requests that the examiner provide an affidavit as set forth in 37 C.F.R. § 104(d)(2).

The fact of the matter is that Chen does not suggest or provide any motivation for one skilled in the art to try his compounds as inhibitors of SCD with a reasonable expectation of success. Thus, even if one assumes, *arguendo*, that the compounds of the invention and compounds of Chen are simple positional isomers, the fact that compounds of the invention are potent inhibitors of SCD is new and unexpected. Therefore, compounds of the invention would not be obvious over those of Chen because they do possess new and unexpected properties. See *In re Norris* 179 F.2d 970 (C.C.P.A. 1950) and *Sterling Drug Inc. v. Watson*, Comr Pats. (108 USPQ 37), cited by examiner on the pages 6-7 of the Office Action.

For reasons set forth above, Chen cannot render claims 57, 58, 61, and 71 obvious. Accordingly, withdrawal of this rejection is respectfully requested.

Allowable Subject Matter

Claims 10, 11, 13-23, 25, 53, 54, and 56

Applicant thanks the Examiner for allowing claims 10, 11, 13-23, 25, 53, 54, and 56.

Claims 59, 60, and 62-69

Applicant thanks the Examiner for indicating that claims 59, 60, and 62-69 contain allowable subject matter. For reasons set forth above, Applicant respectfully submits that the independent claims, from which these claims depend, are allowable. Therefore, Applicant respectfully defers the re-writing of these claims in independent form.

Conclusion

Applicant believes this reply is fully responsive to all outstanding issues and places this application in condition for allowance. If this belief is incorrect, or other issues arise, the Examiner is encouraged to contact the undersigned or his associates at the telephone number listed below. Please apply any charges not covered, or any credits, to Deposit Account 50-0591, Reference 17243/002001.

Dated: February 11, 2010

Respectfully submitted,

By _____

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